

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2004/001369

International filing date (day/month/year)
29.03.2004

Priority date (day/month/year)
27.03.2003

International Patent Classification (IPC) or both national classification and IPC
A61K33/24, A61K31/28, A61P29/00

Applicant
SANTOSOLVE AS

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/001369

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

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Box No. II Priority

1. ☒ The following document has not been furnished:

- ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).
- ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1-5

because:

- ☒ the said international application, or the said claims Nos. 1-5 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/001369

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|--------------------------|
| Novelty (N) | Yes: Claims | 9,12,13,16 |
| | No: Claims | 1-8,10,11,14,15,17 |
| Inventive step (IS) | Yes: Claims | - |
| | No: Claims | 1-17 |
| Industrial applicability (IA) | Yes: Claims | 6-17; see separate sheet |
| | No: Claims | |

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Re Item III.

Claims 1-5 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V.

For the assessment of the present claims 1-5 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

The following documents are referred to in this communication:

- D1 : US 5 851 556 A (BRETON LIONEL ET AL) 22 December 1998 (1998-12-22)
- D2 : WO 96/19184 A (HAHN GARY SCOTT ; COSMEDERM TECHNOLOGIES (US); THUESON DAVID OREL (US)) 27 June 1996 (1996-06-27)
- D3 : HAHN G S: "Strontium is a potent and selective inhibitor of sensory irritation" DERMATOLOGIC SURGERY, ELSEVIER SCIENCE, NEW YORK, NY, US, vol. 25, no. 9, September 1999, pages 689-694, XP002225553 ISSN: 1076-0512
- D4 : WO 97/48371 A (HAHN GARY SCOTT ; QUICK TIMOTHY W (US); COSMEDERM TECHNOLOGIES (US); T) 24 December 1997 (1997-12-24)
- D5 : US 5 866 168 A (BRETON LIONEL ET AL) 2 February 1999 (1999-02-02)
- D6 : US 6 168 777 B1 (GREFF RICHARD J ET AL) 2 January 2001 (2001-01-02)
- D7 : US 5 258 557 A (VARGAS-GARZA HECTOR) 2 November 1993 (1993-11-02)

NOVELTY

1. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-8, 10, 11, 14, 15, 17 is not new in the sense of Article 33(2) PCT in view of D1-D5.

- 1.1 Document D1 discloses salts of alkaline-earth metals for treating rosacea and/or skin irritation and/or darts and/or pudic erythema and/or dysesthetic sensations and/or sensation of inflammation and/or pruritus of the skin and/or of the mucous membranes. The salt is in particular strontium nitrate or -chloride. Example 22 discloses topical compositions for treating acne comprising strontium chloride and EDTA. Thus D1 anticipates present claims 1-7, 10, 11, 14 and 15.
- 1.2 D2 discloses strontium compositions, especially with strontium chloride, -nitrate or acetate (page 17, 26) but also Sr-EDTA (page 26), for avoiding skin irritation associated with e.g. psoriasis and other skin diseases (page 8). Also pain and irritation due to inflammation is mentioned (page 16). Treatment of pain or irritation in the mouth, due to e.g. canker sores, inflammation etc is also envisaged (page 30). Claimed is also a composition comprising an irritant ingredient and strontium (claims 1, 12, 15, ..). The composition can be anti-acne (claims 38, 40, 41). Thus D2 anticipates present claims 1-7, 10, 11, 14 and 15.
- 1.3 D3 discloses the use of soluble strontium salts to block cutaneous type C nociceptors which, upon stimulation, cause release of various chemicals (e.g. substance P) that produce inflammation at the site of stimulation (neurogenic inflammation). This inflammation mediates conditions such as psoriasis and rheumatoid arthritis. Strontium salts suppress this inflammation (page 693, left column, paragraphs 2, 3). Thus D3 anticipates present claims 1-7, 10 and 17.
- 1.4 D4 discloses chloride, acetate, nitrate but also EDTA salts of strontium (pages 30-31, 37). A challenge is to make the compositions penetrate the skin by using various surfactants and solvents (pages 25-26). Anti acne drugs are envisaged in the formulation (page 37). Thus D4 anticipates present claims 1-8, 10 and 14.
- 1.5 D5 discloses treating e.g. acne rosacea with, amongst others, Sr salts as anti-irritants. Also treatment of psoriasis is envisaged (col. 3; claims 1-7; example 4). Thus D5 anticipates present claims 1-7, 10 and 14.

INVENTIVE STEP

2. The present application does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matter of Claims 1-17 does not involve an inventive step (Rule 65(1)(2) PCT) in view of D1-D7.
- 2.1 D6 discloses chelated forms of, amongst others, strontium. D7 discloses compositions of strontium-90 (radioisotope) comprising DMSO.

- 2.2 Claims 8, 9: Use of various compounds to enhance skin penetration of the strontium compounds is known from e.g. D4. From D7, it is known that DMSO is chemically compatible with strontium. DMSO is a well-known penetration enhancer, which, however, can also cause irritation. On the other hand, e.g. D2 claims compositions comprising an irritant; the irritation is obviated by the strontium component. Thus the use of DMSO as a penetration enhancer does not overcome a technical prejudice and is, in itself, well-known. Claims 8 and 9, in combination with any claim upon which they depend, are therefore considered obvious.
- 2.3 Claims 12, 13: No technical effect seems to be obtained by the use of an excess of chelating agent. The application discloses examples 3, 4, 6, 17 comprising equimolar amounts of strontium component and chelating agent, which are also supposed to achieve the effect(s) of the invention. In optimising the known effect of the known compositions, which is a matter of common practice in the field of pharmaceuticals, a skilled person would arrive, without inventive effort, at optimum ratios and concentrations of the various components.
- 2.4 Claim 16: It is generally known that radiation therapy can give rise to inflammation (e.g. of the skin). Given the fact that the strontium compounds are known from the prior art to combat inflammation associated with various disease states, based on e.g. interference with cutaneous nociceptors, it would take no inventive effort on the part of the skilled person to use the strontium compositions in cases where the inflammation (e.g. of the skin) is due to radiation therapy.
- 2.5 Features of other (dependent) claims are disclosed in the prior art; combinations of such features not explicitly disclosed represent obvious alternatives with respect to that same prior art.